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NAYGN McMaster Chapter Nuclear Case Competition 2025: Alpha-Emitting Isotopes in Medicine

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Abstract
North American Young Generation in Nuclear (NAYGN) is a non-profit organization founded in 1999 that is dedicated to empowering the next generation of nuclear professionals. The NAYGN McMaster, a student led chapter of the organization at McMaster University, organized this case competition to provide undergraduate students with the opportunity to engage in problem-based learning while tackling current issues in the nuclear industry. This competition fosters collaboration, thoughtful discussion, and innovation, while also offering participants the chance to grow personally and professionally. This year's theme was "alpha-emitting isotopes in medicine." Teams were tasked with identifying and describing the full production cycle of a specific alpha-emitting isotope, other than Actinium-225, including its sourcing, production methods, applications in medicine, and any associated challenges or innovations in the process. After a round of written submissions, the top eight teams presented their research to a panel of judges at the NAYGN Nuclear Case Competition Expo. The judges selected the top four teams, whose abstracts have been published in this abstract booklet. If you would like to learn more about NAYGN McMaster Chapter or the NAYGN Nuclear Case Competition, please visit our Instagram page (@naygn_mcmaster) or email us (naygn@mcmaster.ca).
Disclaimer: The views expressed throughout this case competition and publication are solely those of the competition participants and do not reflect those of NAYGN McMaster, McMaster University, or any other organization.

Keywords: undergraduate research; radiochemistry; nuclear chemistry; medical isotopes; undergraduate case competition; alpha-emitting isotopes in medicine

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First Place

Thorium-227 – Lifecycle and Potential for Oncological Applications: A Research Study

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The potential applications of radiopharmaceuticals in the medical field remain a critical research interest in the 21st century. From cancer therapy to radio-imaging, the possibilities of radionuclides continue to expand, with many isotopes still being researched. Among these is Thorium-227, an alpha-emitting isotope with strong clinical application potential due to its high linear energy transfer and localized effects. Methodologies of 227Th production comprise decay and separation. 227Th is a decay product of 227Ac, which is produced via neutron irradiation of a 226Ra target in a nuclear reactor. 226Ra is in turn an intermediate product in the decay chain of 238U. 227Th is harvested from a generator that contains 227Ac. Separation columns make it possible to separate and purify the thorium from actinium and radium, removing both the mother and daughter nuclides. The purified thorium may be used on-site or shipped for further use. Research conducted did not suggest that Canada currently produces any meaningful quantities of 227Th. However, Canada has the capability to produce 227Th independently, already being a major exporter of uranium and an investor in nuclear energy with 19 operable nuclear reactors. These nuclear reactors with 238U provide the pathway required to produce 227Th. At the end of the 227Th degradation pathway, it forms a series of unstable elements that emit both gamma rays and X-rays. Gamma rays can pass through the human body, ionizing structures with energy. The energy they contain is bled off with 2-3 inches of lead, or a few feet of concrete. Although these emissions are problematic, the last element of the pathway is a stable Lead-207 isotope. Lead-207 is nonreactive and easily disposed of with an alkaline surfactant. Packaging and transportation of 227Th falls under the Government of Canada's Packaging and Transport of Nuclear Substances Regulations. 227Th classification and subsequent packaging regulations depend upon the relative activity level and radiological hazard of the packaged material, which could present hurdles in clinical applications where larger quantities and activity levels are required. Still, thorium's classification is akin to many other radioactive materials where transportation has always been an industry-wide problem. Therefore, the packaging and transportation of 227Th does not present any special concern. Clinical application of 227Th lies in oncology where it is used in targeted alpha therapy (TAT); its diagnostics are measured via SPECT and uptake estimations made with the MEW-PDQ formula. 227Th's high linear energy transfer allows it to induce complex double-strand DNA breaks. Moreover, unlike other radioisotopes like 223Ra, 227Th can be readily chelated and has a long half-life of ~18.7 days. This allows radiolabeling of tumor-targeting moieties to produce targeted thorium conjugates, which deliver potent alpha radiation to a broad spectrum of tumors. Pre-clinical studies targeting CD22 (a B-cell malignancies marker) and CD33 (an internalized transmembrane glycoprotein) in lymphoma and acute myeloid leukemia have shown promising anti-tumor activity, further supporting the potential of 227Th-based TAT for these cancers.

Second Place

Harnessing Production of Astatine-211 for Advancing Targeted Alpha Therapy: A Research Study

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Since the 1950s, Astatine-211 has been recognized as a promising α-emitter for targeted-alpha therapy. Currently, it is being investigated for potential therapeutic use for thyroid cancers, malignant pheochromocytomas, and ovarian cancers, among others. Additionally, it is being looked at for reducing late complications and early toxicity in hematopoietic cell transplant cases. The production of 211At involves the irradiation of 209Bi with the nuclear reaction 209Bi(α, 2n)211At, using a cyclotron to bombard 209Bi with 28–29 MeV α-beam energies. While it is possible to produce 211At with α-beams energies of 21-40+ MeV, the yield could vary. Furthermore, unwanted 210At and 210Po can be produced at higher energies. As a result, the beam energy should be controlled at 28–29 MeV to optimize yield while minimizing byproduct production. Cooling systems play a vital role in preventing the melting and evaporation of bismuth and astatine during irradiation. A

significant limitation of 211At production is the availability of cyclotrons capable of generating α-beam energies beyond 25 MeV. However, newer cyclotrons, such as the TR-ALPHA manufactured in Canada, are being designed to save on financial and spatial resources while producing large quantities of 211At. The purification of 211At involves dissolving the bismuth target in nitric acid before undergoing a chromatographic separation and extraction. Research has discovered that 211At binds to ketones, a property which distinguishes them from their bismuth precursor. The extraction process involves loading the extract in columns containing 2M or 6M HNO_3, followed by an extraction chromatography using columns filled with beads impregnated with 1-octanol or 3-octanone. This process ensures that >95% of the 211At is retained within the column until stripped with ethanol. This process can be completed in under 30 minutes, taking roughly 10 minutes for the dissolution and 20 for the chromatographic separation. The bismuth is typically extracted from lead-bismuth deposits, which are heated with slag-forming agents (such as SiO_2) at 500-1200ºC. This causes the lead to form a slag and run off, leaving a semi-finished bismuth product behind at around 60-70% purity by weight. Then, it is heated at 500-1200ºC with phosphate-containing flux that decomposes into P_2O_5, while the lead slag runs off, producing 80-90% pure bismuth by weight. The slag runoff can be heated again to retrieve leftover bismuth. Once the bismuth product is collected, it is treated with chlorine gas to convert the leftover lead to lead chloride, which can be separated from the bismuth product. After the purification of 211At, the remaining byproducts include 207Bi and 210At, which are capable of decaying into toxic 210Po and stable 207Pb. These byproducts are typically classified as low-level radioactive waste for isolation, containment, and burying at near surface facilities by agencies like the Nuclear Waste Management Organization. The 211At produced can be transported in containers built from steel with depleted uranium or lead as shielding, such as Type B containers certified by the Canadian Nuclear Safety Commission.

Third Place

Applications of Radium-223 in Advancing Targeted Alpha Therapy for Bone Metastases: A Research Study

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Radium-223 (^{223}Ra) is an isotope of radium that undergoes α-decay with a half-life of 11.4 days. ^{223}Ra can be recovered from ^{235}U decay, but this process is both time consuming and limited in its application. A more efficient method of ^{223}Ra synthesis involves the decay chain of Actinium 227 (^{227}Ac) through a ^{227}Ac-^{227}Th-^{223}Ra generator. To obtain the ^{227}Ac required for synthesis, natural ^{226}Ra is irradiated with neutrons to initiate the ß-decay reaction of ^{227}Ra-^{227}Ac. ^{227}Ac is inserted into a solution along with ^{227}Th and ^{223}Ra, where the charge difference between the isotopic cations ($^{227}Ac^{3+}$, $^{227}Th^{4+}$, and $^{223}Ra^{2+}$) result in the formation of negatively charged species with nitrate ions allow for facilitated separation using ion exchanger materials. ^{227}Ac and ^{227}Th are extracted with a 1M HCl solution and deposited on a column containing a strong anion-exchange resin. While ^{227}Ac and ^{227}Th are selectively retained, ^{223}Ra is recovered using a solution of 1M HNO_3 and concentrated on an AG 50W-X12 cation exchange resin to be recovered with 8M HNO_3 solution, evaporated, and dissolved in a sodium chloride/citrate solution. One other method of separation involves the elution of ^{227}Ac and ^{227}Th using an AG1-X8 column, producing a high purity ^{223}Ra product without disturbing the ^{227}Ac/^{227}Th equilibrium. These methods enable efficient production of ^{223}Ra for research and new targeted alpha therapies. ^{223}Ra dichloride ($^{223}RaCl_2$) is a calcium-mimetic with the ability to specifically target bone lesions, acting as a calcium analog after being injected intravenously. Hydroxyapatites are naturally occurring calcium-phosphate mineral complexes located in human and animal bones, providing them with their structural stability and hardness. Hydroxyapatites are able to form through malignancies in cell cultures through alkaline phosphatase and calcium, enhancing tumor proliferation. Previous preclinical trials show ^{223}Ra's ability to substitute for calcium in hydroxyapatite complexes at sites of active mineralization and formation of metastatic lesions via osteoblasts. Radium's α-radiation causes localized cytotoxicity, leading to DNA helix breaks in adjacent cells, osteoblasts, and osteoclasts, disrupting the positive feedback loop and leading to the inhibition of tumor growth. Patients suffering from mCRPC and bone metastases in the ALSYMPCA (ALpharaAdin in SYMPtomatic Prostate CAncer) trial were treated with injections of either ^{223}Ra or placebo, and those injected with ^{223}Ra had overall longer survival times (median 14.9 vs 11.3 months). The results from this study demonstrate the potential of ^{223}Ra's clinical effectiveness towards cancer treatment via targeting of bone metastases. When examining the toxicity of ^{223}Ra in mice, the isotope was administered intravenously in the form of dissolved radium dichloride. It was found that the unbound compound is cleared primarily through the intestinal route. In conclusion, ^{223}Ra has shown its effectiveness as an α-particle emitting isotope for cancer therapy in both animal and clinical trials.

Fourth Place

Radium-223 as an Alpha-Emitting Isotope Medical Treatment for Bone-Related Cancer Growth: A Research Study

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Targeted alpha therapy is the use of highly energetic radioisotopes to attack and kill cancer cells in targeted tissues. It functions through an alpha-decay pathway where an unstable parent nucleus emits an alpha particle to release energy and transform into a different nucleus. Among current medical isotopes, Radium-223 emerges as a prominent isotope to study due to its clinical usage and ability to fight osteoblastic bone metastases. Radium-223 is a radiotherapy treatment delivered via injection, mimicking calcium's structure to enter bone metastases. Within bone cells, it releases large amounts of energy via a 6-step decay reaction producing Lead-207 as a product. Overall, the emitted energy in the decay series is 28.2 MeV with 95.3% of that energy originating from alpha radiation. Radium-223 is a by-product of Actinium-227 decay. The production of Actinium-227 occurs through neutron irradiation of Radium-226. Radium-226 can be obtained from the decay series of Uranium-238, a metal naturally found in the environment. Canada is the world's second largest supplier of Uranium, accounting for 15% of global supplies in 2022. Thus, obtaining Uranium-238 or Radium-226 is realistic. Uranium-238 bombarded during neutron irradiation becomes Uranium-239, as it gains a neutron. Since Uranium-239 undergoes beta decay, it becomes Plutonium-239 which can be used as fuel in nuclear reactors. Neutron irradiation occurs where a material is bombarded with neutrons. This can be done at the neutron irradiation facility, TRIUMF, in British Columbia. First, an aluminum plate is exposed to a proton beam, with energies ranging from 120-480 MeV. Then, the neutrons produced are concentrated into a neutron beam, which is shot at Radium-226 producing Actinium-227. The purification and extraction of Radium-223 from Actinium-227 can be done with an anion exchange resin in a chromatography column. The column of unpurified Radium-223 is washed three times with water, eluted with 80% methanol, and 0.4M nitric acid. Eluted Radium-223 is then put on a hot plate to evaporate the nitric acid. Finally, it is combined into a solution of sodium chloride and sodium citrate to produce radium dichloride ($^{223}RaCl_2$), the clinically used radium salt. Radium-223 can be transported over long distances and periods due to its 11.4-day half-life and has no radiation shielding requirements, as it does not emit harmful radiation. While in transport, it should be kept in a sealed glass vial within a lead container. Post-treatment, Radium-223 is disposed in a clinical radioactive waste stream. Due to the stable nature of Radium-223, the transport and storage are less problematic in contrast to other radioisotopes. The use of Radium-223 is the only bone-directed treatment for tumours and cancer cells. This leads to prominent clinical applications in both primary (cancer originating in bones) and secondary bone cancers (cancer metastasizing to bones, notably, prostate cancers). The administered dose is lower than other prevalent radiopharmaceuticals and is fully compliant with regulatory standards for cancer treatment. Additionally, Radium-223 has no restrictions on interpersonal contact, mitigating cancer-related psychosocial challenges. With respect to the presence of Radium-223 in Canada, it is worth investigating as a potential radioisotope for bone-related cancer growths.

Conflicts of Interest
The authors declare no conflict of interests.

Authors' Contributions
AE: Founded the 1st annual NAYGN McMaster Chapter Nuclear Case Competition, served on the planning committee of the case competition, drafted the case competition abstract booklet, and gave final approval of the version to be published.
PH: Served on the planning committee of the case competition and gave final approval of the version to be published.
KBA: Served on the planning committee of the case competition and gave final approval of the version to be published.
MC: Founded the 1st annual NAYGN McMaster Chapter Nuclear Case Competition, served on the planning committee of the case competition, and gave final approval of the version to be published.

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